

IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

1. (Currently Amended) Process for preparing cephadine, said process comprising reacting 7- aminodesacetoxy cephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form (DH_a) in the presence of an enzyme in a reaction mixture to form cephadine, resulting in a conversion of 7-ADCA into cephadine of at least 70 %, wherein the concentration D-dihydrophenylglycine (DH) in the reaction mixture is below 2wt. % throughout the reaction; wherein ~~throughout the reaction if said enzyme is a wild type penicillin acylase said reacting is carried out at a temperature below 15°C, or if said enzyme is an acylase having a higher S/H ratio than the wild type acylase of E.coli throughout the reacting step and said reacting is carried out at a temperature of at least 15°C.~~
2. (Previously Presented) Process according to claim 1, wherein said reacting results in a conversion of 7-ADCA into cephadine of at least 80%.
3. (Previously Presented) Process according to claim 1, wherein said reacting results in a conversion of D-dihydrophenylglycine in activated form (DH_a) into cephadine (CEF) of at least 70%, wherein

the conversion of DH_a into CEF = $(n_{CEF}/ n_{DH_a}) *100\%$;
 n_{CEF} = quantity of cephadine formed (in mole); and
 n_{DH_a} = total quantity of DH_a added to reaction mixture (in mole).
4. (Currently Amended) Process according to claim 1, wherein the concentration DH in the reaction mixture is maintained below 2 wt. %, throughout said reacting by controlling the pH of the reaction mixture between pH 6 and 9 ~~and/or when said enzyme is a wild type penicillin acylase said reacting is carried out at a temperature between -5 and 15°C, or when said enzyme is an acylase having a higher S/H ratio than the wild type~~

~~acylase of E.coli~~ wherein said reacting is carried out at a temperature of between 15 and 35°C.

5. (Previously Presented) Process according to claim 1, wherein the sum of the quantity of 7-ADCA added to the reaction mixture and DHa added to the reaction mixture is between 10 and 2000 mmol per liter of reaction mixture.

6. (Previously Presented) Process according to claim 1, characterized in that dihydrophenylglycine in activated form is dihydrophenylglycine methylester.

7. (Previously Presented) Process according to claim 1, characterized in that dihydrophenylglycine in activated form is a HCl salt of dihydrophenylglycine methylester.

Claims 8-10 (canceled)

11. (Previously Presented) Process according to claim 1, characterized in that the enzyme is immobilized on a carrier.

12. (Previously Presented) Process according to claim 1, wherein the process is a batch process.

Claims 13-14 (Canceled)

15. (Previously Presented) Process according to claim 1, wherein said reacting is carried out at a pH of at least 7.0.

Claim 16 (Canceled)

17. (Previously Presented) Process according to claim 1, wherein said reacting is carried out at a pH of below 7.7.

18. (Previously Presented) Process according to claim 1, characterized in that the enzyme is a mutant penicillin acylase is derived from a wild type acylase via recombinant DNA methodology by substituting one amino acid residue for a new residue.

19. (Currently Amended) Process according to claim 1, wherein the process comprises crystallizing the cephadine from an aqueous solution to form cephadine hydrate with a water content between 3% and 6% by weight.

20. (Previously Presented) Process, according to claim 19, said process comprising:

reacting aminodesacetoxy cephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form (DH_a) in the presence of an enzyme in a reaction mixture to form cephadine; and

crystallizing the cephadine from an aqueous solution, in which aqueous solution the ratio $m_{CEF}/(m_{7\text{-ADCA}} + m_{CEF}) > 0.7$, preferably > 0.8 , more preferably > 0.9 , and wherein XDH = 0-2 wt. %, preferably 0-1 wt. %, wherein

m_{CEF} = molar quantity of cephadine in the aqueous solution;

$m_{7\text{-ADCA}}$ = molar quantity of 7-ADCA in the aqueous solution; and

XDH = concentration of DH in the aqueous solution relative to the total weight of the aqueous solution.

21. (Previously Presented) Process according to claim 19, wherein the process comprises separating the enzyme from the cephadine prior to said crystallizing.

22. (Previously Presented) Process according to claim 1, wherein the concentration 7-ADCA in the aqueous solution is between 0 and 5 wt. %.

23. (Previously Presented) Process according to claim 19, wherein said crystallizing is performed at a temperature of between 45 and 60 °C.

24. (Currently Amended) Process for preparing cephadine hydrate crystals with a water content between 3% and 6% by weight, characterized in that the process comprises crystallizing cephadine from an aqueous solution to form cephadine hydrate, wherein said crystallizing is carried out at a temperature of between 45 and 60°C.

25. (Previously Presented) Process according to claim 19, wherein said crystallizing is performed at a pH of between 4.0 and 6.0.

26. (Currently Amended) Process for the preparation of cephadine characterized in that the process comprises:

- reacting 7-aminodesacetoxy cephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form in the presence of an enzyme in a reaction mixture to prepare cephadine; and
- crystallizing the cephadine from an aqueous solution to form cephadine hydrate with a water content between 3% and 6% by weight according to the process according to claim 24.

27. (Previously Presented) Process according to claim 1, wherein part of the cephadine formed is crystallized and present in the reaction mixture as cephadine hydrate, and wherein the process further comprises dissolving at least part of said cephadine hydrate in said reaction mixture.

28. (Previously Presented) Process according to claim 27, wherein said dissolving is effected at a pH of above 8.

29. (Canceled).

30. (Previously Presented) Process according to claim 1 characterized in that said reacting is carried out in the presence of sodium bisulphite.

Claims 31-32 (Canceled).